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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/995,911	11/28/2001	Richard B. Mazess	017620-9335	4126

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EXAMINER	
WILLIAMS, LEONARD M	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 07/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/995,911	MAZESS, RICHARD B.	
	Examiner	Art Unit	
	Leonard M. Williams	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *56-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *04/15/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 56-60 and 63-71 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 5763429. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-9 of '429 detail a method of inhibiting the hyperproliferative activity of human prostatic neoplastic or hyperplastic cells by administration of a variety of vitamin D compounds of formula (I). Claim 3 of the '492 patent discloses vitamin D species that are identical to the species detailed in the current application's claims 4 and 5. Claim 8 of the '492 patent teaches a method wherein the vitamin D compound is administered in a mixture including a second anticancer agent selected from the group estramustine phosphate, prednimustine,

cisplatin, 5-fluoro-uracil, melphalan, hydroxyurea, mitomycin, idarubicin, methtrexate, adriamycin, and daunomycin.

The '492 patent does not teach the method of inhibiting hyperproliferation of malignant or neoplastic cells broadly, nor does it teach cancers other than prostate. The '492 patent does not teach the vitamin D dosage as being 10μg to 200μg/ dose given once per week to once every 12 weeks.

It would have been obvious at the time the invention was made that the compounds of '492 could be used in the treatment of any cancer cells that expressed the vitamin D receptor, additionally the claim language is simply broadening the scope of claims 1 and 2 of the '492 patent. The allowed broad claims 1 and 2 of patent '492 are not limited to a particular dosage regiment and thus place the vitamin D dosage of the current application within the boundaries of the '492 claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 56-58, 61, and 67-71 are rejected under 35 U.S.C. 102(a) as being anticipated by Dore et al. (US Patent No. 5547947) as evidenced by Goodman and Gilman's The Pharmaceutical Basis of Therapeutics, 7th edition.

Dore et al. teach, in col. 1 lines 45-65, a method of inhibition or loss of cell proliferation in solid tumors by administration of a vitamin D3 analog such as 1α,25-dihydroxy-26,27-hexafluorocholecalciferol alone or in combination with trans retinoic acid. Dore et al. teach, in col. 6 lines 10-25, that the vitamin D3 analog is to be administered in amounts from 0.00025-0.01 mg (0.25-10 μg) per day (1.75-70 μg per week) with the trans retinoic acid in the range of 1-20mg per day anticipating the "...method of inhibiting proliferation of malignant or neoplastic cells, comprising treating the cells with...an active vitamin D compound...wherein the amount of active vitamin D is...between about 10mg to about 200mg/dose given once per week to once every 12 weeks" of claim 56, the "...method ...wherein the malignant cells are associated with cancers..." of claim 57, the "...method...wherein the hypocalcemic vitamin D compound is a compound of formula (III)..." of claim 58 and the "...method...wherein the active vitamin D lacks a hydrocarbon moiety at the C-24 position" of claim 61, the "...method inhibiting hyperproliferation of malignant or neoplastic cell, comprising...co-administering...an active vitamin D compound and an...antineoplastic agent a bone agent, an antihypercalcemic agenent or combinations..." of claim 67, the"...method...are episodically co-administered..."of claim 68, the "...method...wherein the agent is an antineoplastic agent" of claim 69, the "...method...whereinthe antineoplastic agent...and the active vitamin D is given concurrently..." of claim 70, and the "...method...wherein

the antineoplastic agent is...or any other antineoplastic agent or combinations thereof" of claim 71.

Goodman and Gilman's The Pharmaceutical Basis of Therapeutics, 7th edition teaches on pages 1573-1580, that the retinoids (including retinol, retinal, and retinoic acid) have activity as anticancer agents. On page 1580 it is disclosed that following the binding of retinoic acid to the CRABP complex in the cytosol the complex migrates inducing a cascade of specific biochemical events. Correlation has been found between the CRABP and the antitumor effects of the retinoids.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 72-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dore et al. as applied to claim 56-58; 61, and 67-71 above, and further in view of Schwender et al. (US Patent 5300687).

Dore et al. is as set forth above.

Dore et al. does not teach a method wherein the bone agent is a bisphosphonate, nor a method wherein a vitamin D compound, an antineoplastic agent, and an antihypercalcemic agent are co-administered.

Schwender et al. teaches, in col. 1 lines 22-30, that osteoporosis treatments include estrogen replacement, bisphosphonates, vitamin D metabolites and calcium supplements.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use bisphosphonates in conjunction with the vitamin D and retinoic acid compounds of Dore et al. as the bisphosphonates are known compounds useful in the treatment of bone disorders.

The examiner respectfully points out the following from MPEP 2144.06: "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re* Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Claim 62 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dore et al. (US Patent No. 5547947) as applied to claims 56-58, 61, and 67-71 above, and further in view of Suda et al. (US Patent No. 4391802).

Dore et al. is as set forth above.

Dore et al. does not teach 1α,25-dihydroxyvitamin D_3 or 1α-dihydroxyvitamin D_3.

Suda et al. teach, in the abstract and experiment 5, a method of treating leukemia or a leukemoid disease by administration of a vitamin D derivative (1α,25-dihydroxyvitamin D_3).

It would have been obvious at the time the invention was made to use the vitamin D derivatives of Suda et al. (including 1α,25-dihydroxyvitamin D_3) in Dore et al.'s method of inhibition or loss of cell proliferation in solid tumors by administration of a vitamin D_3 as both the solid tumors and the leukemia cells have vitamin D receptors and are thus modulated by vitamin D as vitamin D and its derivatives must be internalized in order to effect a cellular response in normal cells as well as malignant cells, without evidence to the contrary.. One would have been motivated to use 1α,25-dihydroxyvitamin D_3 as it is one of the active metabolites of vitamin D_3 (see Suda et al. col. 1 lines 10-25). One would have expected a reasonable chance of success as both methods are targeted toward the same vitamin D_3 receptor using derivatives of vitamin D_3 and are directed toward the treatment of hyperproliferative states (i.e. cancer).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leonard M Williams whose telephone number is 571-272-0685. The examiner can normally be reached on MF 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LMW

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER